Appendix D

Categorical Regression Analysis

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Guth and associates (1991) described an alternative quantitative method to estimate a chemical concentration associated with a low probability of observable adverse effects. The method uses categorical regression analysis of the probability of a group of exposed subjects demonstrating a statistically significant adverse effect relative to control subjects. The adverse effects are divided into three severity categories: No Observed Adverse Effect Level (NOAEL), Adverse Effect Level (AEL), and Frank Effect Level (FEL); AEL and FEL categories are combined for the analysis. Experimental observations from various species may be depicted on the same plot to determine whether certain species are more sensitive than others to the toxicological effects of exposure to a particular chemical. The form of the modeled concentration-duration-response relationship is:

$$Ln(p/1\text{-}p) = \alpha + \beta_1 * Ln(C) + \beta_2 * T$$

> where p is the probability of observing an AEL or FEL
> α is the intercept parameter
> β_1 and β_2 are slope parameters
> C is the exposure concentration
> T is the exposure duration.

A data set for a given experimental concentration and duration associated with a p=0.1 for an AEL/FEL response is estimated to be associated with a 10% probability of being categorized as an AEL/FEL data set and a 90% probability of being categorized as a NOAEL data set. This method of analysis takes into account the experimental duration and concentration, eliminating the need to perform any further time extrapolation (i.e., with the formula $C^{n} {}^{*} T = K$) as is done with the NOAEL and BD methods.

While this method has not been formally adopted by OEHHA or USEPA, it has potential applications that may make it the preferred one under some circumstances. This method allows the information from a large number of smaller studies reporting NOAEL or LOAEL data to be combined and therefore strengthens the conclusions reached.

Figure D-1 depicts a plot of the categorical regression of acute human and rat central nervous system effects resulting from exposure to a hypothetical chemical. Data are presented on a log concentration vs. linear duration axis. Each separate dose group in each study is depicted by a single point. An acute toxicity exposure level for this chemical could be derived from the dose at which exposures are predicted to result in a probability of 0.1 that an AEL would be observed (the EC_{10}).
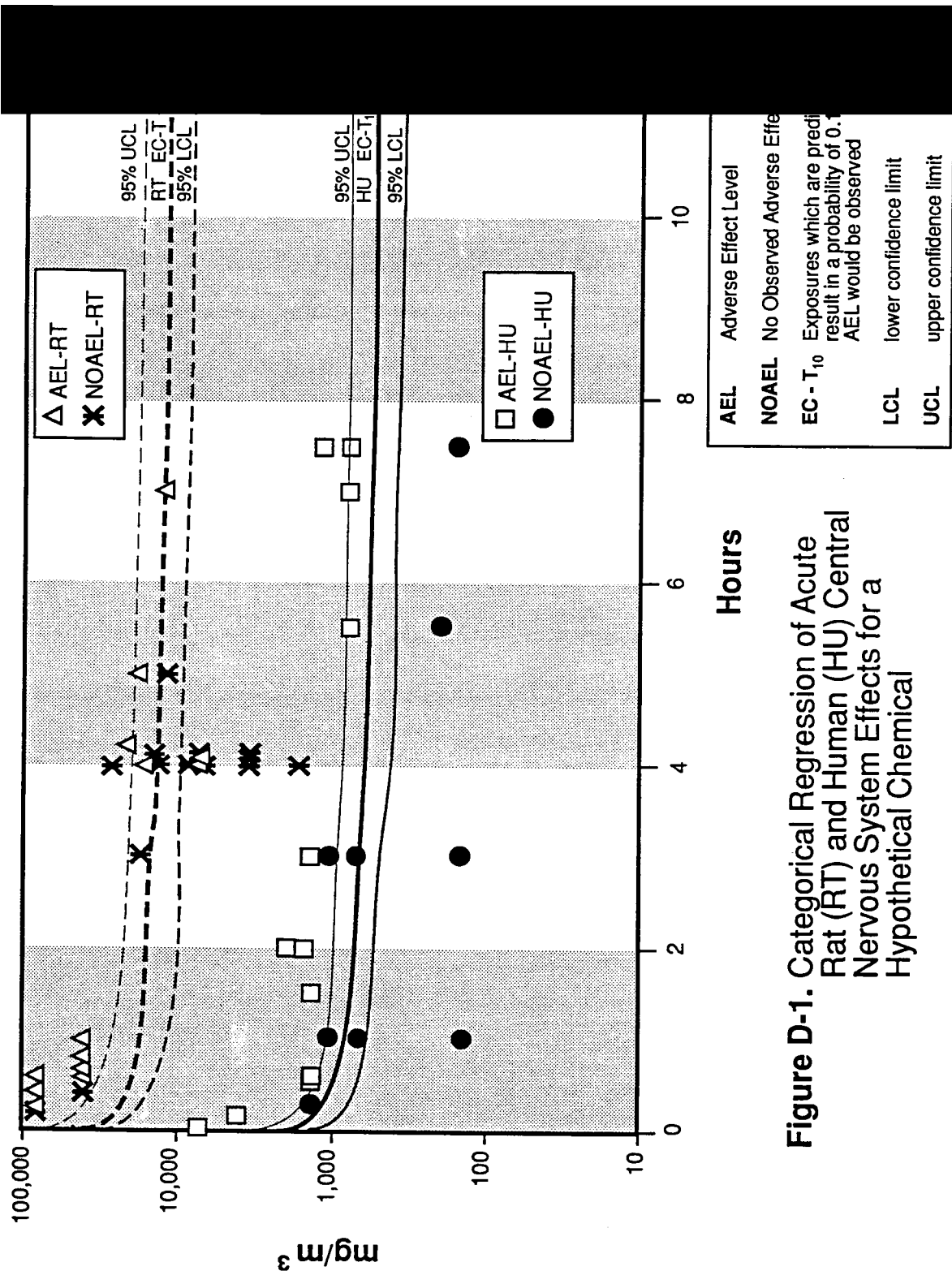
Figure D-1. Categorical Regression of Acute Rat (RT) and Human (HU) Central Nervous System Effects for a Hypothetical Chemical